

Amendments to the Specification:

Please replace paragraph **[0011]** beginning at page 7, line 14, with the following:

--**[0011]** The invention also provides specific siRNA molecules for inhibition of expression of cell cycle genes. In one embodiment, the invention provides a CK2-specific siRNA molecule comprising the sequence AACATTGAATTAGATCCACGT (SEQ ID NO:37). The CK2-specific siRNA molecule can be from 21 to 30 nucleotide base pairs in length. In one aspect, the CK2-specific siRNA molecule has the sequence AACATTGAATTAGATCCACGT (SEQ ID NO:37) and its complement as active portion. The CK2-specific siRNA molecules can be used in a method of inhibiting expression of a CK2 gene in a cell, by contacting the cell with the method comprising contacting the cell with a CK2-specific siRNA molecule from 21 to 30 nucleotide base pairs in length that includes the sequence AACATTGAATTAGATCCACGT (SEQ ID NO:37).--

Please replace paragraph **[0012]** beginning at page 7, line 23, with the following:

--**[0012]** In another embodiment, the invention provides a PIM1-specific siRNA molecule comprising the sequence AAAACTCCGAGTGAAGTGGTC (SEQ ID NO:38). The PIM1-specific siRNA molecule can be from 21 to 30 nucleotide base pairs in length. In one aspect, the PIM1-specific siRNA molecule has the sequence AAAACTCCGAGTGAAGTGGTC (SEQ ID NO:38) and its complement as active portion. The PIM1-specific siRNA molecules can be used in a method of inhibiting expression of a PIM1 gene in a cell, by contacting the cell with the method comprising contacting the cell with a PIM1-specific siRNA molecule from 21 to 30 nucleotide base pairs in length that includes the sequence AAAACTCCGAGTGAAGTGGTC (SEQ ID NO:38).--

Please replace paragraph [0013] beginning at page 8, line 1, with the following:

--[0013] In another embodiment, the invention provides a ~~Hbo1-specific an HBO1-specific~~ siRNA molecule comprising the sequence AACTGAGCAAGTGGTTGATT (SEQ ID NO:39). The ~~Hbo1-specific HBO1-specific~~ siRNA molecule can be from 21 to 30 nucleotide base pairs in length. In one aspect, the ~~Hbo1-specific HBO1-specific~~ siRNA molecule has the sequence AACTGAGCAAGTGGTTGATT (SEQ ID NO:39) and its complement as active portion. The ~~Hbo1-specific HBO1-specific~~ siRNA molecules can be used in a method of inhibiting expression of a ~~Hbo1 an HBO1~~ gene in a cell, by contacting the cell with the method comprising contacting the cell with a ~~Hbo1-specific an HBO1-specific~~ siRNA molecule from 21 to 30 nucleotide base pairs in length that includes the sequence AACTGAGCAAGTGGTTGATT (SEQ ID NO:39).--

Please replace paragraph [0037] beginning at page 9, line 27, with the following:

--[0037] Figure 23 provides amino acid sequences (SEQ ID NOS:40 and 41) for dominant negative mutants of CDC7L1.--

Please replace paragraph [0038] beginning at page 10, line 1, with the following:

--[0038] Figure 24 provides amino acid sequences (SEQ ID NOS:42 and 43) for dominant negative mutants of CNK.--

Please replace paragraph [0039] beginning at page 10, line 2, with the following:

--[0039] Figure 25 provides amino acid sequences (SEQ ID NOS:42 and 43) for dominant negative mutants of STK2.--

Please replace paragraph **[0040]** beginning at page 10, line 3, with the following:

--[0040] Figure 26 provides an alternative view of the amino acid sequences (SEQ ID NOS:40 and 41) for dominant negative mutants of CDC7L1.--

Please replace paragraph **[0052]** beginning at page 11, line 3, with the following:

--[0052] Figure 38 demonstrates that expression of IRES Hbø1 HBO1 E508Q is antiproliferative in A549 cells.--

Please replace paragraph **[0053]** beginning at page 11, line 5, with the following:

--[0053] Figure 39 demonstrates that no significant differences in proliferation are observed between Hbø1 HBO1 WT and mutant proteins when expressed in H1299 cells.--

Please replace paragraph **[0054]** beginning at page 11, line 7, with the following:

--[0054] Figure 40 demonstrates that expression of Hbø1 HBO1 mutant E508Q is antiproliferative in HeLa cells.--

Please replace paragraph **[0055]** beginning at page 11, line 9, with the following:

--[0055] Figure 41 depicts analysis of proliferation in sorted cells that express wild type or mutant Hbø1 HBO1 proteins.--

Please replace paragraph **[0072]** beginning at page 12, line 18, with the following:

--**[0072]** Figure 58 demonstrates that expression of the Ape1 APE1 D210A mutant sensitizes A549 cells to methyl methanesulfonate treatment.--

Please replace paragraph **[0073]** beginning at page 12, line 20, with the following:

--**[0073]** Figure 59 demonstrates that wild type Ape1 APE1 and the Ape1 APE1 C65A mutant are protective when expressed in A549 cells treated with bleomycin.--

Please replace paragraph **[0074]** beginning at page 12, line 22, with the following:

--**[0074]** Figure 60 demonstrates that wild type Ape1 APE1 and the Ape1 APE1 C65A mutant are protective when expressed in HeLa cells or H1299 cells treated with bleomycin.--

Please replace paragraph **[0076]** beginning at page 12, line 27, with the following:

--**[0076]** Figure 62 provides the sequence sequences (SEQ ID NOS:51 and 52) of dominant negative mutants of CK2 α . Consensus peptides = SEQ ID NOS:53 and 54.--

Please replace paragraph **[0079]** beginning at page 13, line 4, with the following:

--**[0079]** Figure 65 provides the sequence sequences (SEQ ID NOS:55 and 34) of dominant negative mutants of NKIAMRE.--

Please replace paragraph **[0080]** beginning at page 13, line 5, with the following:

--[0080] Figure 66 provides the sequence sequences (SEQ ID NOS:57, 63 and 64) of dominant negative mutants of FEN1. Consensus peptides = SEQ ID NOS:58-62 and 65-68.--

Please replace paragraph **[0083]** beginning at page 13, line 10, with the following:

--[0083] Figure 69 provides the sequence sequences (SEQ ID NOS:34 and 20) of dominant negative mutants of CDK3.--

Please replace paragraph **[0086]** beginning at page 13, line 19, with the following:

--[0086] Figure 72 provides the sequence sequences (SEQ ID NOS:69 and 70) of dominant negative mutants of HBO1.--

Please replace paragraph **[0087]** beginning at page 13, line 20, with the following:

--[0087] Figure 73 provides the sequence sequences (SEQ ID NOS:42 and 71) of dominant negative mutants of PIM1. Consensus peptides = SEQ ID NOS:72-75.--

Please replace paragraph **[0098]** beginning at page 16, line 17, with the following:

--[0098] REV1 encodes a 1251 amino acid dCMP transferase that functions in the Pol ζ mutagenesis pathway (*see, e.g.*, Lui *et al.*, *Nuc. Acids. Res.* 27(22):4468 (1999) and Zhang *et al.*, *Nuc. Acids Res.* 30(7):1630 (2002)). REV1 has been implicated in UV induced mutagenesis repair and is postulated to play a role in UV damage tolerance (*see, e.g.*, Murakomo, *J. Biol.*

Chem., 276(38):35644 (2001)). dCMP transferase assays known to those of skill in the art can be used to identify modulators of REV1 (*see, Zhang et al.*, 2002 and *J. Biol. Chem.*, 276(18):15051). For example, dCMP, 5'-end 32P-labeled oligonucleotide primer 5'-CACTGACTGTATG-3' (SEQ ID NO:76) annealed to an oligonucleotide template, 5'-CTCGTCAGCATCTTCAUCATACAGTCAGTG-3' (SEQ ID NO:77) treated with uracil-DNA glycosylase may be used as substrates in assays to identify modulators of REV1 (*see, e.g., J. Biol. Chem.*, 276(18):15051).--

Please replace paragraph **[0226]** beginning at page 62, line 31, with the following:

--**[0226]** Common linkers such as peptides, polyethers, and the like can also serve as tags, and include polypeptide sequences, such as poly gly Gly sequences of between about 5 and 200 amino acids (SEQ ID NO:78). Such flexible linkers are known to persons of skill in the art. For example, poly(ethylene glycol) poly(ethylene glycol) linkers are available from Shearwater Polymers, Inc. Huntsville, Alabama. These linkers optionally have amide linkages, sulfhydryl linkages, or heterofunctional linkages.--

Please replace paragraph **[0282]** beginning at page 80, line 21, with the following:

--**[0282]** CK2 activity can be measured according to the method described in Messenger *et al.*, *J. Biol. Chem.*, 277(25):23054 (2002). Briefly, cell extracts are incubated in 1 mM of a synthetic peptide substrate, RRRDDDSDDD (SEQ ID NO:79) in 20 mM Tris-HCl pH 7.5, 60 mM NaCl, 10 mM MgCl₂, 1 mM DTT, and 100 μM γ-32P-ATP. After an appropriate incubation, the reactions are stopped, run on SDS-PAGE, and phosphorylated proteins are detected by bioimaging analysis.--

Please replace paragraph **[0301]** beginning at page 84, line 22, with the following:

--[0301] Hbø1 HBO1 mutants were constructed with the following mutations: Hbø1 HBO1 G484E, Hbø1 HBO1 L497S, and Hbø1 HBO1 E508Q. Hbø1 HBO1 mutants are shown in Figure 72. Both wild type and mutant Hbø1 HBO1 proteins were localized to the cell nucleus. (Data not shown.)--

Please replace paragraph **[0302]** beginning at page 84, line 25, with the following:

--[0302] The effect of Hbø1 HBO1 expression on tumor cell lines was determined using cells that had been infected with a retrovirus that expressed Hbø1 HBO1 wild type or mutant proteins. The Hbø1 HBO1 E508Q mutant was antiproliferative in A549 cells (IRES only) and HeLa cells (GFP fusion and IRES construct) and had no effect in H1299 cells. Expression of the wild type Hbø1 HBO1 protein and the other mutants had no effect on proliferation in this assay. See, e.g., Figures 38-40. Additional assays were performed using only sorted GFP positive cells as shown in Figure 41. Proliferation was measured using the CyQuant Cell Proliferation Assay (Molecular Probes) which is based upon the fluorescence enhancement upon binding of a proprietary dye to cellular DNA. Using sorted cells, the Hbø1 HBO1 E508Q mutant was strongly antiproliferative in A549 cells and HeLa cells. See, e.g., Figures 42-43.--

Please replace paragraph **[0303]** beginning at page 85, line 4, with the following:

--[0303] An Hbø1 HBO1 siRNA caused greater than 50% reduction in mRNA expression when transfected into A549 cells or H1299 cells. The sequence of the Hbø1 HBO1 siRNA is as follows: AACTGAGCAAGTGGTTGATT (SEQ ID NO:39). The Hbø1 HBO1 siRNA had an antiproliferative effect when expressed in A549 or H1299 cells. See, e.g., Figures 44-45.--

Please replace paragraph **[0305]** beginning at page 85, line 16, with the following:

--[0305] PIM1 mutants were constructed with the following mutations: Pim1 PIM1 K67A and PIM1 D186N. PIM1 mutants are shown in figure 73.--

Please replace paragraph **[0307]** beginning at page 85, line 25, with the following:

--[0307] A PIM1-specific siRNA caused greater than 50% reduction in mRNA expression when transfected into A549 cells, HeLa cells, or H1299 cells. The sequence of the PIM1 siRNA is as follows: AAAACTCCGAGTGAAC~~T~~GGTC (SEQ ID NO:38). The PIM1 siRNA had an antiproliferative effect when expressed in A549, HeLa cells, or H1299 cells. See, *e.g.*, Figures 51-53. In primary HUVEC cells the PIM1-specific siRNA caused greater than 50% reduction in mRNA expression and had an antiproliferative effect. See, *e.g.*, Figure 54.--

Please replace paragraph **[0315]** beginning at page 87, line 8, with the following:

--[0315] A CK2 α -specific siRNA caused greater than 50% reduction in mRNA expression when transfected into H1299 cells. The sequence of the CK2 α -specific siRNA (also know as CK2) is as follows: AACATTGAATTAGATCCACGT (SEQ ID NO:37). The CK2 α siRNA had an antiproliferative effect when expressed in H1299 cells. See, *e.g.*, Figure 63. The same CK2 α siRNA reduced mRNA in HeLa cells but did not appear to effect cell proliferation. (Data not shown.)--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 79, at the end of the application.